HSI Health Sciences Investigations Journal

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ISSN Online 2704-4890 | ISSN Print 2720-7609

Online first publication

Original Research Article

HSI Journal (2024) Volume 6 (Issue 2):918-926. https://doi.org/10.46829/hsijournal.2024.12.6.2.918-926

Open Access

The effect of combined vaginal misoprostol and tourniquet or tourniquet alone on reducing blood loss during abdominal myomectomy: a randomised controlled trial

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Received September 2024; Revised October 2024; Accepted November 2024

Abstract

Background: Uterine fibroids are common benign tumours in women, with myomectomy being a primary surgical treatment for those desiring to preserve fertility. This procedure is often associated with significant haemorrhage. Both the tourniquet and misoprostol are effective at reducing the associated blood loss, and their combined use may enhance this effect.

Objective: The study aimed to compare blood loss reduction using vaginal misoprostol plus a tourniquet versus a tourniquet alone during abdominal myomectomy.

Methods: This study was an open-label randomised controlled investigation involving 80 women with symptomatic fibroids, divided into two groups: the treatment group (misoprostol plus tourniquet) and the control group (tourniquet alone). The primary outcome measured was intraoperative blood loss through changes in haemoglobin levels. Secondary outcomes included the need for blood transfusion, postoperative febrile morbidity, surgery duration, misoprostol's adverse effects, and length of hospital stay. The treatment group received a single 600µg dose of vaginal misoprostol one hour before surgery. Data analysis utilised SPSS version 22, employing t-tests for continuous variables and Chi-squared tests for categorical variables, with a significance threshold of $p < 0.05$.

Results: Results indicated a significant reduction in blood loss (haemoglobin change) when misoprostol plus tourniquet was used for uterine sizes ≥ 18 weeks (1.40 ± 0.50 vs 1.89 ± 0.80 g/dl, $p = 0.005$). However, there were no significant differences in blood transfusion need (2.5% vs 5.0%, $p = 0.55$), febrile morbidity (2.5% vs 2.5%, $p = 0.99$), surgery duration (102.73 ± 36.02 vs 104.08 ± 40.04 min, $p = 0.874$), or hospital stay length (2.88 ± 0.607 vs 3.05 ± 0.714 days, $p = 0.241$). Misoprostol adverse effects were minimal (10% in the treatment group).

Conclusion: A 600µg vaginal misoprostol dose plus a tourniquet significantly reduces blood loss during abdominal myomectomy for uterine sizes ≥ 18 weeks compared to a tourniquet alone, with similar transfusion requirements, surgery duration, febrile morbidity, and hospital stay lengths.

Keywords: Tourniquet, misoprostol, abdominal myomectomy, haemorrhage

Cite the publication as Agyabeng DAA, Saka E, Seffah JD, Ndanu T, Swarray-Deen A (2024) The effect of combined vaginal misoprostol and tourniquet or tourniquet alone on reducing blood loss during abdominal myomectomy: a randomised controlled trial. HSI Journal 6 (2):918-926. https://doi.org/10.46829/hsijournal.2024.12.6.2.918-926

INTRODUCTION

Uterine leiomyoma is the most common benign genital tract tumour in women of reproductive age, and it is usually one of the common reasons why women make gynecologic visits to the 37 Military Hospital. These tumours are estrogen-dependent and originate from myometrial smooth muscle cells [1]. Uterine fibroids are mostly asymptomatic, with incidental discovery during a pelvic examination or ultrasound for other indications [2]. Symptomatic uterine fibroid can adversely affect the

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quality of life of a woman, and symptoms may include menorrhagia, pelvic pain or pressure, abdominal distension, as well as urinary and bowel complaints [3]. Uterine fibroids may also be associated with reproductive problems, including impaired fertility, pregnancy complications, and loss, as well as adverse obstetric outcomes [4].

Current management strategies mainly involve surgical interventions, but the choice of treatment is guided by the patient's age and desire to preserve fertility or otherwise [3]. The definitive treatment for symptomatic uterine fibroids is hysterectomy for women who do not desire to preserve their fertility [5]; however, myomectomy is performed if preservation of fertility is desired. Surgical and non-surgical approaches include myomectomy by hysteroscopy, abdominal myomectomy by laparotomy or laparoscopy, uterine artery embolisation, and interventions performed under radiologic or ultrasound guidance to induce thermal ablation of the fibroid nodules [6,7]. Compared with laparotomy, laparoscopic myomectomy has the advantages of small incisions, short hospital stays, less postoperative pain, rapid recovery, and good assessment of other abdominal organs [8]. Laparoscopic myomectomy should be performed by surgeons with expertise in laparoscopic surgeries. Although failure to suture the uterine incision properly may be associated with an increased risk of future uterine rupture, reports in the available literature concerning uterine rupture have been conflicting [9]. Due to the lack of surgical expertise in laparoscopic surgeries, the current practice at the 37 Military Hospital is to perform all abdominal myomectomy procedures using laparotomy.

Haemorrhage is one of the most common complications in women undergoing myomectomy [10]. Controlling haemorrhage during myomectomy continues to be a serious challenge confronting the gynaecologist. Several options have been described and promoted over the years to achieve this goal. These include both preoperative and intraoperative interventions used to minimise blood loss, such as the use of tourniquets, clamps, intraoperative vasopressin, tranexamic acid, and use of gonadotrophin-releasing hormone (GnRH) agonists or aromatase inhibitors [11]. Newer agents, such as selective progesterone receptor modulators (Ulipristal acetate), have been used as preoperative interventions in myomectomy [12]. The use of these preoperative medications, however, may potentially result in a loss of tissue plane and, consequently, the difficult enucleation of the fibroid nodules [13]. Misoprostol, commonly known as Cytotec, has also been used to reduce blood loss during abdominal myomectomy in recent times [14]. It is a synthetic prostaglandin E1 analogue approved by the USA Food and Drugs Authority (FDA) about 30 years ago for treating gastric ulcers. It is commonly used for cervical ripening, induction of labour, first and second-trimester terminations, as well as management of postpartum haemorrhage [14]. In a study published by Abdel-Hafiz et al. in 2015, it was shown that a single preoperative dose of rectal misoprostol (400 ug) significantly reduced intraoperative blood loss with the drop in postoperative haemoglobin levels being significantly less compared with placebo [15]. However, results from a study conducted in Nigeria involving the use of either vaginal misoprostol or intraoperative tourniquet showed that the reduction in blood loss was comparable between the two groups [16]. This study, therefore, sought to assess the effect of the combined use of vaginal misoprostol and tourniquet compared with tourniquet alone during abdominal myomectomy.

MATERIALS AND METHODS

Study design

This was an open-label, parallel randomised controlled study conducted with misoprostol plus tourniquet as the treatment group and tourniquet alone as the control group, with an allocation ratio of 1:1.

Sample selection

Eligibility criteria for participants included all reproductive-aged women with symptomatic fibroids who desire future fertility with uterine size not exceeding 28 weeks of gestation on abdominal examination (most of the myomectomies in the department are performed on uterine sizes not exceeding 28 weeks of gestation) and who gave voluntary consent to partake in the study. However, participants were excluded when any of the following were present: Parous reproductive-aged women with symptomatic fibroids and no future fertility wishes; perimenopausal women with symptomatic fibroids who do not desire fertility; women with haemoglobinopathies levels less than 10 g/dL before surgery; women with prior abdominal surgeries including caesarean section and previous myomectomy; women with body mass index (BMI) greater than 35 kg/m^2 due to surgical challenges; women who refuse blood transfusion; women with hemoglobinopathies and coagulation disorders; women with co-existing chronic medical conditions; women who have allergies to prostaglandins; and women with symptoms suggestive of COVID-19 and who tested positive for the SARS-CoV-2 virus within the two-week period before surgery. All women with symptomatic uterine fibroids scheduled for myomectomy at the Division of Obstetrics and Gynaecology at the 37 Military Hospital were recruited. Participants were sampled randomly using systematic random sampling after determining the sampling frame (interval), which is stated in the study as 2.

Interventions

Group 1 (the intervention group) received vaginal misoprostol (600 µg) administered into the posterior fornix at least one hour before surgery, in addition to the peri-cervical tourniquet. Group 2 (the control group) received only the peri-cervical tourniquet, which is the standard practice at the 37 Military Hospital. The misoprostol used was sourced from the Maternity Pharmacy, and the brand used was Cytotec, which was produced by Pfizer

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Pharmaceuticals. It was stored at room temperature, not exceeding 30 ºC, as recommended by the manufacturer. Before surgery, all participants received 1 litre of normal saline prior to spinal anaesthesia as part of standard practice. Both groups used peri-cervical tourniquets with a size 18 Foley catheter, tied at the cervical-isthmic junction of the uterus before the uterine incision, under strict aseptic conditions. The fallopian tubes and ovaries were excluded from the tourniquet to prevent compression and necrosis. Fibroid nodules were removed using traction and counter-traction with minimal uterine incisions. The tourniquet was finally removed after repair of the uterus and confirmation of hemostasis. Uterine incisions were closed in layers using absorbable Vicryl sutures, minimising knots on the serosal surface.

Hemostatic sutures were added as needed. The peritoneal cavity was cleaned, and the abdomen was closed in layers using Vicryl for transverse incisions or Nylon for midline incisions. The abdominal wound was cleaned with alcohol-soaked gauze and covered with dry gauze and plaster. The perineum was cleaned, and suppository analgesics like paracetamol or diclofenac were used for postoperative pain management. Urine output was measured and recorded. Participants were nursed in the recovery ward for about an hour before transferring to the main gynaecology ward for further management. All drug administration was performed by the same resident on the gynaecology ward an hour before surgery. Participants were identified by code number and underwent standard preoperative evaluations, including complete blood count, urinalysis, serum electrolyte, urea, creatinine, and pelvic ultrasound for leiomyoma assessment. One certified sonographer conducted ultrasounds to avoid inter-observer bias. Other investigations were done as needed. Four experienced Specialist Gynaecologists, each with at least four years of experience, performed the procedure. All the surgeons performed an equal number of surgeries. Blood transfusion (intraoperative/ postoperative) was commenced in the presence of cardiovascular instability, signs of inadequate perfusion or oxygenation, when the postoperative haemoglobin was less than 7g/dL, or when there were symptoms of anaemia after surgery despite haemoglobin level greater than 7 g/dL.

Outcomes

The primary outcome, blood loss, was estimated by measuring preoperative and postoperative haemoglobin levels. All participants had haemoglobin levels measured 24 hours after surgery as part of routine postoperative care. This involved drawing 2 ml of venous blood for a full blood count, performed using flow cytometry. Blood samples were taken by the same resident who administered the pre-surgery drugs. None of the participants underwent hysterectomy, and there were no instances of lost follow-up among the study participants. Secondary outcomes assessed in this study included the need for blood transfusion, postoperative febrile morbidity, surgery duration, length of hospital stay, and adverse effects of misoprostol. Adverse effects were evaluated within one hour of drug administration to 24 hours after the surgery.

Sample Size

The primary outcome measure for the study is the level of blood loss, which is measured as a reduction in haemoglobin. The level of blood loss was compared between treatment and control groups. The reported blood loss in the treatment group was x1, and that in the control group was x2. A study by Srivastava et al. using changes in haemoglobin levels compared the blood loss for women in the treatment group (vasopressin plus rectal misoprostol) as against the control group (vasopressin alone) and reported blood loss of 139 ± 96.7 ml for the treatment group and 206 ± 101.2 ml for the control group. The standard deviation for the treatment group was 96.7. Applying the formula below:

$n = 2\sigma^2(Zcrit + Zpwr)^2/D^2$
which was derived from a previously validated formula.55
n is the sample size per group.

σ (standard deviation) = 96.7
Zcrit = 1.96 (Z-score value for 95% confidence level)
Zpwr = 0.842 (Z-value at statistical power of 80% or 0.8)
x1= 139 and x2= 206
D = x1-x2 = difference in blood loss
Sample size calculation:
$n = 2x96.7^2(1.96+0.842)^2$
$(139-206)^2$
n = 32.7

The sample size obtained was 32.7, which is approximated to 33. Adding an attrition rate of 10% gave a sample size of 36.3, which was rounded up to 40 participants per group and a total of 80.

Randomisation

The study used systematic randomisation with a sampling interval of 2, determined by dividing the number of eligible participants (133) by the sample size (80). The number of eligible participants was obtained by accessing the hospital records to determine all women who had been scheduled for myomectomy and who met the inclusion criteria. The first participant was randomly assigned to either Group 1 or Group 2 by picking a labelled paper from an opaque envelope, and the second participant was assigned to the alternate group. This sequence continued until all participants were recruited. The random allocation sequence was generated by the principal investigator and was concealed from all participants until interventions were assigned. Participants were enrolled and assigned to interventions with the help of two research assistants. All four operating surgeons were blinded to group allocations to minimise any biases during surgery.

Statistical Methods

Data was collected using a structured questionnaire and data collection form, with security ensured by a computer-based feature. The data was cleaned in Microsoft Access and analysed in SPSS version 22. Analysis was by intention-to-treat. Categorical variables were summarised

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using frequencies and proportions, while continuous variables were summarised using mean and standard deviation. Specifically, blood loss reduction, surgery duration, and hospital stay length were summarised as means and standard deviations. Adverse effects and blood transfusion needs were summarised as proportions and presented in tables. An independent t-test was used to compare blood loss reduction between the two groups, with statistical significance set at $p < 0.05$ and a 95% confidence interval.

RESULTS

A total of 133 women were screened for eligibility in the study. Out of this number, 60.2% (n = 80) of the women were randomly selected to participate in the study, with 40 women in each group. Participants for the study were recruited from 12th April 2021 to 1st December 2021. They were followed up for six weeks per the standard practice for all women who undergo major gynaecological surgeries at 37 Military Hospital. No participant was lost to follow-up. The trial ended after the last participant in the study completed her follow-up. The mean age of the participants in both groups was comparable (35.38 ± 5.75 vs 37.33 ± 5.00 years, p = 0.118). The age was normally distributed, with actual ages ranging between 23 - 47 years. Most of the participants were single (53.8%, n = 43) and nulliparous (72.5%, n = 58), with parous women making up 27.5% (n = 22) of the study population. Approximately half of the study participants (45%, n = 36) had their education at the tertiary level. The common presenting symptoms were abnormal uterine bleeding (28.7%, n = 23), infertility (12.5%, n = 10), pelvic pain (11.2%, n = 9), and 40.3% (n = 32) multiple symptoms. The majority of the participants were Christians (90%, n = 72), with only 10% (n = 8) of participants being Muslims (Table 1). There were similarities in the two groups concerning mean uterine size (22.50 ± 4.12 vs 21.35 ± 4.11 weeks, p = 0.215) and the mean number of fibroid nodules removed (21.33 ± 18.57 vs 20.05 ± 15.22, p = 0.738). All participants were given spinal anaesthesia.

The two main abdominal incisions used were Pfannenstiel and sub-umbilical midline incisions, with 71.3% (n = 57) having Pfannenstiel incisions and 28.7% (n = 23) having sub-umbilical midline incisions. None of the participants had a sub-umbilical midline incision with an extension above the umbilicus. (Table 2). There was no significant

Table 1. Sociodemographic characteristics of the study population

Variables	Group 1, n = 40	Group 2, n = 40	Total, n = 80 (%)	p-value
Age groups (years)				0.118
≤25	3	-	3 (3.8)	
26- 30	6	6	12 (15.0)	
31-35	9	11	20 (25.0)	
36-40	17	11	28 (35.0)	
≥41	5	12	17 (21.2)	
Mean ± standard deviation	35.38 ± 5.75	37.33 ± 5.00	36.35±5.44	
Marital status				0.717
Single	23	20	43 (53.7)	
Married	13	15	28 (35.0)	
Divorced	4	4	8 (10.0)	
Widowed	-	1	1 (1.3)	
Educational status				0.121
None	-	1	1 (1.3)	
Primary school	1	4	5 (6.3)	
Junior High School (JHS)	13	5	18 (22.4)	
Senior High School (SHS)	8	12	20 (25.0)	
Tertiary	18	18	36 (45.0)	
Parity				0.409
0	32	26	58 (72.5)	
1	6	9	15 (18.7)	
2	2	4	6 (7.5)	
3	-	1	1 (1.3)	
Presenting complaints				0.327
Abnormal uterine bleeding	9	14	23 (28.7)	
Pelvic pain	4	5	9 (11.2)	
Abdominal distension	3	0	3 (3.8)	
Infertility	6	4	10 (12.5)	
Urinary/ Bowel symptoms	3	0	3 (3.8)	
Multiple symptoms	15	17	32 (40.0)	
Religion				0.263
Christianity	38	34	72 (90.0)	
Islam	2	6	8 (10.0)	

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Table 2. Intra-operative events of participants in the two groups

Variable	Group 1, n = 40 (%)	Group 2, n = 40 (%)	χ^2 / t	p value
Uterine size (weeks)				
12-16	3 (33.3)	6 (66.7)		
18-22	19 (48.7)	20 (51.3)	1.526	0.466
24-28	18 (56.3)	14 (43.8)		
Mean ± standard deviation	22.50 ± 4.12	21.35 ± 4.11	1.562	0.215
Anesthesia				
Spinal	80 (100.0)	80 (100.0)	-	-
General	-	-		
Skin incision				
Pfannenstiel	27 (67.5)	30 (75.0)	0.549	0.459
Sub-umbilical midline	13 (32.5)	10 (25.0)		
Sub-umbilical midline+extension above the umbilicus	-	-	-	-
Location of fibroids				
Submucousnadd	23 (57.5)	30 (75.0)	2.739	0.098
Intramural	39 (97.5)	40 (100.0)	1.013	0.314
Subserous	29 (72.5)	22 (55.0)	2.650	0.104
Number of fibroids				
Submucous	27.26 ± 21.06	20.77±15.83	1.644	0.206
Intramural	22.03 ± 18.73	20.05±15.22	0.263	0.610
Subserous	25.07 ±20.11	24.68±17.14	0.005	0.943
Mean ± standard deviation	21.33±18.57	20.05±15.22	0.113	0.738

Table 3. Pre-operative, Intra-operative, and postoperative management

Variable	Group 1, n = 40, (%)	Group 2 n =40, (%)	χ^2 / t	p-value
Estimated blood loss				
Pre-op Hb	11.78 ± 1.19	11.86 ± 1.03		0.727
Post-op Hb	10.39 ± 1.31	10.15 ± 1.06		0.374
Mean ± standard deviation	1.39 ± 0.60	1.71 ± 0.86	3.822	0.054
Blood transfusion				
Yes	1 (2.5)	2 (5.0)	0.346	0.556
No	39 (97.5)	38 (95.0)		
Number of units transfused				
1	1	-		
2	-	2		
≥ 3	-	-		
Mean ± standard deviation	0.02±0.15	0.05±0.22	0.339	0.562
Post-operative monitoring				
Febrile morbidity	1 (2.5)	1 (2.5)		0.99
Length of hospital stay (days)				
2	9 (60.0)	6 (40.0)	1.600	0.449
3	28 (50.0)	28 (50.0)		
≥4	3 (33.3)	6 (66.7)		
Mean ± standard deviation	2.88 ± 0.61	3.05 ± 0.71	1.394	0.241
Uterine size				
≥ 18 weeks	37	34		
Change in hemoglobin				
Mean ± standard deviation	1.40 ± 0.59	1.89 ± 0.80		0.005

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Table 4. Adverse effects of misoprostol among group 1 participants

Variable	Frequency n = 40 (%)
Nausea	
Yes	0 (0.0)
No	40 (100.0)
Vomiting	
Yes	0 (0.0)
No	40 (100.0)
Shivering/ Chills	
Yes	3 (7.5)
No	37 (92.5)
Abdominal cramps	
Yes	1 (2.5)
No	39 (97.5)

difference in the mean duration of surgery between the treatment and control groups (102.73 ± 36.02 vs 104.08 ± 40.04 min, p = 0.874). There was a comparable mean preoperative haemoglobin level (11.78 ± 1.19 vs 11.86 ± 1.03 g/dl, p = 0.727) and mean postoperative haemoglobin level (10.39 ± 1.31 vs 10.15 ± 1.06 g/dl, p = 0.374) between groups 1 and 2 respectively. The intraoperative blood loss as measured by the mean difference between preoperative and postoperative haemoglobin levels was lower in group 1 participants (treatment group) than in group 2 participants (control group), but this was not statistically significant (1.39 ± 0.60 vs 1.71 ± 0.86 g/dl, p = 0.054). However, when uterine size ≥ 18 weeks was compared to the change in haemoglobin level between group 1 and group 2, there was a change in haemoglobin level in group 1 than in group 2 and this was statistically significant (1.40 ± 0.59 vs 1.89 ± 0.80 g/dl, p = 0.005). The number of participants in both groups who received postoperative blood transfusion was comparable (2.5% vs 5.0%, p = 0.55) as well as the mean number of blood transfused (0.2 ± 0.15 vs 0.5 ± 0.22; p = 0.562).

However, none of the participants in both groups received intraoperative blood transfusion. Mean postoperative temperature readings e (36.75 ± 0.39 vs 36.90 ± 0.23, p = 0.10). Postoperative febrile morbidity was recorded in two participants, one in each group (2.5% vs 2.5%; p = 0.99). The length of hospital stay compared between the two groups was found to be less in group 1 than in group 2, but this was not statistically significant (2.88 ± 0.607 vs 3.05 ± 0.714 days, p = 0.241). One participant (2.5%) in group 1 was readmitted after discharge on account of pelvic abscess. However, all participants had a good level of satisfaction despite one participant being readmitted (Table 3). Adverse effects of misoprostol were recorded in 10% (n = 4) of participants in group 1 (Table 4).

DISCUSSION

The main objective of this study was to determine the reduction in blood loss when misoprostol was combined with a tourniquet or when a tourniquet was used alone in women undergoing abdominal myomectomy. Misoprostol has been reported to be effective in reducing blood loss during myomectomy following comparison with other agents [16] or placebo [15] or following adjunctive use with other agents [19]. Tourniquet has also been reported to be effective in reducing blood loss during myomectomy, following a comparison with other agents [16] and adjunctive use with other agents [20]. The mean change in haemoglobin level following adjunctive use of misoprostol with a tourniquet in this study was lower than the mean change in haemoglobin level following adjunctive use of tranexamic acid with a tourniquet in a randomised controlled trial by Abdul et al. where they recorded a value of 1.44 ± 0.73 g/dl [20]. A review of the methodology of the study involving the adjunctive use of tranexamic acid with a tourniquet revealed similar sample size, exclusion, and inclusion criteria compared with this study. However, the lower mean change in haemoglobin in this study may be due to the uterotonic effect of misoprostol, which acted as a chemical tourniquet during periods of release of the cervical-isthmic tourniquet, an effect deficient with tranexamic acid. In addition, the mean change in haemoglobin of the misoprostol group recorded in this study was also lower than the mean change in haemoglobin following adjunctive use of misoprostol and vasopressin in a randomised, double-blind, controlled study by Frederick et al. [19] (1.39 ± 0.60 vs 1.6 ± 1.5 g/dl). Although intramyometrial injection of vasopressin, when used alone, is more effective than the solitary use of tourniquet at reducing blood loss by causing less reduction in haemoglobin during myomectomy [21], this is not the case when misoprostol is used as adjunctively with either tourniquet or vasopressin. This may be explained by the higher dose of misoprostol and the vaginal route of misoprostol used in this study.

Furthermore, the mean change in haemoglobin in the misoprostol group from this study was much lower than reported in a study conducted in Egypt by Abdel-Hafeez et al. [15] (1.39 ± 0.60 vs 1.7 ± 0.4 g/dl). The difference may be explained by several factors in this study: misoprostol was used adjunctively with pericervical tourniquet, the dose used was 600 µg (as compared to 400 µg), and the route of administration was vaginal (as compared to rectal). Different studies have used different dosing regimens for misoprostol in myomectomy, as well as different routes of administration. Dosages of 200 µg [22], 400 µg [16], 600 µg (present study), and 800 µg [23] have been used in various studies, with different outcomes in the change in haemoglobin levels.

Different routes of administration of misoprostol have been used in the literature, but the vaginal route has been shown to have a wider area under the curve. In a study by Khan et al. on route-dependent pharmacokinetics of misoprostol, vaginal misoprostol was present in the circulation longer than oral misoprostol and had a greater area under the curve at 240 minutes (p < 0.001). Rectal misoprostol had a similar pattern but a much lower area under the curve at 240

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minutes, thereby showing that misoprostol is absorbed best when administered vaginally [24], hence its use in this study. Misoprostol caused a significant reduction in intraoperative blood loss in this study when the uterine size was ≥ 18 weeks by causing a smaller change in haemoglobin levels ($p = 0.005$). This may be due to the higher dose of misoprostol used. Moreover, misoprostol has also been shown to significantly reduce the volume of uterine fibroids [25]. Almost all participants in the misoprostol group had uterine sizes ≥ 18 weeks, except for only three participants. Uterine size > 16 weeks is associated with significant bleeding during myomectomy [26], therefore, the use of misoprostol during myomectomy will help to further reduce fibroid volume and blood loss. In addition, a study by Pundir et al. showed that a uterine size of 20 weeks' size and above is associated with significant bleeding ($p < 0.02$) during myomectomy [27]. A uterine size ≥ 18 weeks used in this study was therefore comparable to the uterine sizes used by the studies above. Moreover, a systematic review and meta-analysis showed a similar result that misoprostol use presented significantly smaller changes in haemoglobin levels ($p < 0.001$) [14]. However, most of the studies included in the above meta-analysis used lower doses of misoprostol, and their mean uterine sizes were also significantly smaller compared to the mean uterine size in the treatment group of this study.

This study had no requirement for intraoperative blood transfusion, contrary to reports of 60% [16] and 24% [15] rates of intraoperative blood transfusion from other studies. Furthermore, the need for postoperative blood transfusion was similar between this study's misoprostol and control groups and was not statistically significant. This may be due to the fact that the misoprostol group in this study had a tourniquet as an adjunct. There is no consensus on the time to initiate blood transfusion during myomectomy. In this study, however, intraoperative blood transfusion was to be commenced in the presence of cardiovascular instability from haemorrhage or signs of inadequate perfusion or oxygenation, which was similar to the criteria used by Afolabi et al. in Nigeria [16]. A similar outcome was reported in a systematic review and meta-analysis conducted by Iavazzo et al., in which misoprostol was compared to a placebo, and there was no difference in the need for blood transfusion [14]. Comparing the control groups in this study and the meta-analysis cited above, a significant difference in blood transfusion was expected in the meta-analysis because a tourniquet (as used in this study) is more effective at reducing blood loss than a placebo. Moreover, the need for postoperative blood transfusion was similar in a randomised controlled study by Afolabi et al. (participants were transfused in the presence of cardiovascular instability from haemorrhage or signs of inadequate perfusion or oxygenation) [16] compared to this study. In this study, postoperative blood transfusion was commenced when participants had postoperative haemoglobin < 7 g/dl or were symptomatic of anaemia despite haemoglobin > 7 g/dl or in the presence of cardiovascular instability, but the study by Afolabi et al. stated no postoperative haemoglobin value below which transfusion was to be commenced.

Despite these similarities in postoperative blood transfusion with the above studies, the mean number of units transfused in this study was lower. The mean number of units transfused in the misoprostol plus tourniquet group in this study was lower than the mean number of units in the tranexamic acid plus tourniquet group in a study by Abdul et al. [20] (0.2 ± 015 vs 0.75 ± 1.28 units). Moreover, comparing the mean number of units transfused among the control groups (tourniquet only) of these two studies, there were lower mean numbers in this study compared to the study by Abdul et al. [20] (0.5 ± 0.22 vs 1.13 ± 1.64 units). These differences, however, were not significant, and no reasons could be attributed to them.

The duration of surgery varies widely in the available literature when either misoprostol or tourniquet is used alone or as adjuncts to other methods. The mean duration of surgery in the misoprostol plus tourniquet group reported in this study is significantly lower compared to that reported in the study using tranexamic acid plus tourniquet [20] (102.73 ± 36.02 vs 157.63 ± 47.66 mins). In addition, a similar significantly lower mean duration of surgery was observed in the control group of this study compared to the control group of the above study (104.08 ± 40.04 vs 158.43 ± 68.24 mins). However, these differences could not be attributed to any reason. In contrast, a study conducted in Nigeria by Afolabi et al. reported a lower mean duration of surgery in the tourniquet-only group [16] compared to what was reported in the tourniquet-only group of this study (102.13 ± 38.76 vs 104.08 ± 40.04 mins). The difference could be due to the higher mean number of fibroid nodules removed in this study (20.05 ± 15.22 vs 11.45 ± 8.22 nodules). In the same study, the misoprostol group had a longer mean duration of surgery (109.48 ± 34.90 mins) [16] compared to the misoprostol group in this study (102.73 ± 36.02 mins). Furthermore, a study from Iran reported a relatively longer mean duration of surgery (106 ± 29 mins) with misoprostol compared to this study [22]. These differences in the duration of surgery may be explained by the additional effect provided by the tourniquet to misoprostol in this study, which helped to reduce blood loss further and hasten the surgical procedure.

Adverse misoprostol effects reported in this study were minimal and self-limiting. The commonest reported in this study were shivering (7.5%) and abdominal cramps (2.5%), which occurred in 10% of participants in the misoprostol group. Shivering was managed by keeping the participants warm with blankets, although it was self-limiting. However, the abdominal cramps were managed with IV Paracetamol. None of the participants experienced other misoprostol side effects, such as nausea, vomiting, pyrexia, or diarrhoea, and no participant experienced multiple adverse effects. This study compared the adverse effects of misoprostol to a Nigerian study by Afolabi et al. [16], which

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reported a similar incidence of shivering. However, the overall number of participants experiencing adverse effects was lower in this study than in the Nigerian study (10% vs 17.5%). This was unexpected given the higher dose of misoprostol used in this study relative to the study by Afolabi et al. A randomised, double-blind, placebo-controlled trial in Egypt reported an overall adverse effect of misoprostol in 44% of participants, but a smaller number experienced shivering (8%). [15] This was an unexpected outcome, considering the lower dose of misoprostol used. Despite achieving a significant reduction in blood loss, fewer adverse effects were reported in this study compared to previous studies. This result is contrary to the findings of a study by Ragab et al., which showed that a higher dose of misoprostol directly impacts the severity of adverse effects [23]. Febrile morbidity after surgery is an important symptom that needs to be well managed because it might delay recovery. Postoperative febrile morbidity was similar between the two groups in this study, with no statistical significance. This may be due to the use of regular IV paracetamol in the first 24 hours after surgery, which may mask febrile morbidity despite its occurrence in 2 participants. A systematic review and meta-analysis have reported similar outcomes concerning postoperative febrile morbidity [14].

The length of hospital stay between the intervention and control groups in this study was comparable, with no statistical significance. Similar outcomes have been reported in a study conducted in Egypt by Abdel-Hafeez et al. between the misoprostol and control groups (3.33 ± 0.49 vs 3.33 ± 0.62, $p = 1.00$) [15]. However, the mean number of days in the misoprostol group from this study was relatively lesser than that in the misoprostol group from the above study conducted in Egypt (2.88 ± 0.607 vs 3.33 ± 0.49). This difference may be due to the addition of a tourniquet to the misoprostol group in this study, which resulted in relatively less blood loss, as evidenced by the lower mean change in haemoglobin and may have resulted in a faster recovery and early discharge.

Conclusion

A single preoperative dose of vaginal misoprostol (600 µg) plus peri-cervical tourniquet is a simple and effective method of significantly reducing blood loss during abdominal myomectomy when uterine size is ≥ 18 weeks compared to the use of pericervical tourniquet alone. There was, however, no significant difference in the need for intraoperative or postoperative blood transfusion, febrile morbidity, surgery duration, and length of hospital stay. Additionally, this dosage of misoprostol did not result in any appreciable increase in the adverse effects of the drug. The indirect means of assessing blood loss during abdominal myomectomy was a limiting factor because there are relatively more accurate means of assessing blood loss, such as photometry (Colorimetric method), gravimetric method, and direct measurement. These, however, were not used because they are labour-intensive and time-consuming, making it difficult to adopt in routine clinical practice in a centre with a heavy workload, such as the 37 Military Hospital.

The trial findings indicated that the intervention of adding vaginal misoprostol to the tourniquet during myomectomy contributes significantly to blood loss reduction. Due to the random sampling of participants, the sample was representative of the population of women seen at the gynaecology clinic with symptomatic fibroids not exceeding 28 weeks' size at the 37 Military Hospital, and therefore, the results of the study can be validly generalised to this population of patients within this facility because it was a single-centre study. For a broader generalizability beyond this facility, a multicentre study is needed.

DECLARATIONS

Ethical consideration

The trial was registered with the Pan African Clinical Trial Registry with registration number PACTR202303468069055.

Consent to publish

All authors agreed on the content of the final paper.

Funding

None

Competing Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Author contributions

DAAA and TN were involved in the generation and editing of data for this article. DAAA, ES, JDS and ASD designed the study and drafted the manuscript. Dr DAAA and TN contributed to the editing and interpretation of data.

Acknowledgement

The time made available by the participants is hereby acknowledged.

Availability of data

Data is available upon request to the corresponding author.

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